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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/633,034	08/04/2000	Kwong Y. Tsang	A33081	2330

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/633,034	Applicant(s) TSANG ET AL.	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-50 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-50 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Reissue Applications

1. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,688,657 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

2. Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

3. These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

4. The original patent, or a statement as to loss or inaccessibility of the original patent, must be received before this reissue application can be allowed. See 37 CFR 1.178.

5. Claims 1-50 are pending and under examination. The restriction requirement mailed 6/27/01 has been vacated.

Specification

6. The disclosure is objected to because of the following informalities:

a. The ATCC address in column 4 needs to be updated to indicate the new address is 10801 University Boulevard, Manassas, VA 20110-2209.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-50 are indefinite for reciting "said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions" in claims 1, 30, 34, 38 because the exact meaning of the phrase is not clear. It is not clear what fraction the claimed antigen is contained in. Is the antigen in the membrane fraction? In addition, is the antigen purified away from HL-A antigen and the glycoprotein fraction or is the antigen in the glycoprotein fraction?

b. Claim 33 recites the limitation "a substrate for the enzyme" in claim 30. There is insufficient antecedent basis for this limitation in the claim.

c. Claims 36 and 37 are indefinite because they depend on claims reciting the samething. Claim 36 recites the kit of claim 32 where the reporter is an enzyme and claim 32 recites the reporter is an enzyme. Likewise claim 37 depends on claim 33 which recites the same thing.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 2-6, 17-29, 34-35, 38-41, 43, 47, 49-50 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line which produces an antibody having the exact chemical identity of 33.28, 31.1, or Chi #1 are known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which

produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species 33.28, 31.1, or Chi #1. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

Applicant's referral to the deposit of 33.28, 31.1 in column 3, lines 58 to column 4, lines 1-2 of the patent is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant

of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

11. Claims 1, 7-16, 30-33, 42, 44-46, 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite an antibody specific for a purified human colon carcinoma-associated protein antigen that is characterized by a purification method and the antigen is not detected in normal and is not detected in cells other than colon carcinoma and is immunogenic and induces an immune response. The specification only teaches a 61.1 kD protein and a 72 kD protein with the claimed characteristics. No other antigen are disclosed in the specification. The claims are broadly drawn to any molecular weight protein with the claimed characteristics, however, no other antigens are disclosed as having the claimed characteristics. As such it would reasonable to conclude to one of skill in the art that the inventor(s) at the time of the application was filed did not have in their position the claimed invention.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Herlyn et al (PNAS 76:1138, 3/79).

The claims recite an antibody specific for an antigen characterized by a purification and wherein the antigen is not detected on human carcinoma cells other than colon and is not detected on normal tissue and the antigen is immunogenic in

humans and induces an immune response and is radiolabeled. Because of the indefinite nature of claim 1 (see 112 second above) the claim is interpreted to recite a colon carcinoma antigen that is not in normal cells and in colon carcinoma cells.

Herlyn et al teach antibodies to antigens from colon carcinoma cells and the antibody does not bind to normal cells and the antibody is radiolabled (see abstract and entire document. In addition, it would be inherent that the antigen would induce an immune response in humans because the antigen is not found in normal tissue. Thus the art reads on the claims.

14. Claims 1, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Hollinshead et al (Cancer 56:480-489, 1985).

The claims have been described supra. The interpretation of claim 1 has been described supra.

Hollinshead et al teach monoclonal antibody to a colon carcinoma which induces an immune response (see page 481) and the antigen is not present in normal tissue (see page 487) and the antibody is used in an ELISA (see page 487).

15. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Price et al (IRCS Journal of Medical Science 13:366-367, 1985).

The claim and the interpretation has been described supra.

Price et al teach an antibody to a colon carcinoma antigen wherein the antigen is in colon cacinoma cells and not in normal colon cells (see Table page 367). Since the

antigen is in carcinoma cells and not in normal cells it would be inherent that the antigen induces an immune response in humans.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1, 7-15, 30-33, 36-37, 42, 44, 45, 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hollinshead et al (Cancer 56:480-89, 1985) as applied to claims 1 and 8 above, and further in view of Neuberger et al (WO 86/01533, published 3/86).

Claims 1 and 8 and the interpretation of claim 1 has been described supra. Claims 7, 9-15, 30-33, 36-37, 42, 44, 45, and 48 recite wherein the antibody is radiolabel, on a solid phase, labeled with a cytotoxic radiolabel, a cytotoxic drug or protein, compositions comprising such, the antibody is a chimeric antibody, wherein the antigen is 72 kD and a method of diagnosing comprising removing a specimen and contacting the sample with a chimeric antibody and staining the specimen and detecting the complex.

Hollinshead et al has been described supra. Hollinshead does not teach a chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody. These deficiencies are made up for in the teaching of Neuberger et al.

Neuberger et al teach chimeric antibodies and antibodies that can be labeled with toxins, radiolables, dyes, cytotoxic agents (see page 7) and the antibody can be immobilized for affinity chromatography (see page 8).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Hollinshead et al and Neuberger et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Hollinshead et al and Neuberger et al because Hollingshead et al teach the antigen is of molecular weight of 72 kD and the antigen is a colon carcinoma associated antigen and an ELISA for detection of the antigen in samples was performed and the antibody was labeled with an enzyme. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Hollinshead et al and Neuberger et al because Neuburger et al teach labeling of antibodies for detection and treatment with cytotoxic agents and radiolabels and the antibodies are chimeric antibodies. Thus, it would have been obvious to one of ordinary skill in the art to produce a chimeric antibody which is a labeled antibody to the antigen of Hollinshead in view of Neuberger et al.

Although claim s 30-33 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detectably labeling antibodies and derivatives thereof also were well known and available to the ordinarily skilled artisan.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

18. Claims 1, 7-15, 30-33, 36-37, 42, 45, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herlyn et al (PNAS 76:1138, 1979) or Price et al (IRCS Journal of Medical Science 13:366, 1985) and further in view of Neuberger et al (WO 86/01533, published 3/86).

The claims and the interpretation have been described supra.

Herlyn et al and Price et al have been described supra. Herlyn et al and Price et al do not teach chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody. These deficiencies are made up for in the teaching of Neuberger et al.

Neuberger et al teach chimeric antibodies and antibodies that can be labeled with toxins, rabiolables, dyes, cytotoxic agents (see page 7) and the antibody can be immobilized for affinity chromatography (see page 8).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Herlyn et al or Price et al in view of Neuberger et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Herlyn et al or Price et al et al and Neuberger et al because Herlyn

et al or Price et al teach a colon carcinoma antigen and detection of the antigen. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Herlyn et al or Price et al and Neuberger et al because Neuberger et al teach labeling of antibodies for detection and treatment with cytotoxic agents and radiolabels and the antibodies are chimeric antibodies. Thus, it would have been obvious to one of ordinary skill in the art to produce a chimeric antibody which is a labeled antibody to the antigen of Herlyn et al or Price et al in view of Neuberger et al.

Although claim s 30-33 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detectably labeling antibodies and derivatives thereof also were well known and available to the ordinarily skilled artisan.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

19. No claim is allowed. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Harlow et al ., Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, pages 61, 67, 71, 92-93, 1988.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

21. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879